

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING
OF A CHANGE(PCT Rule 92bis.1 and
Administrative Instructions, Section 422)

Date of mailing (day/month/year) 20 August 2001 (20.08.01)	
Applicant's or agent's file reference PU3650/WO	IMPORTANT NOTIFICATION
International application No. PCT/EP00/03848	International filing date (day/month/year) 28 April 2000 (28.04.00)

From the INTERNATIONAL BUREAU

To:

LEAROYD, Stephanie, A.
GlaxoSmithKline
Corporate Intellectual Property
Two New Horizons Court
Brentford
Middlesex TW8 9EP
ROYAUME-UNI

1. The following indications appeared on record concerning:				
<input type="checkbox"/> the applicant <input type="checkbox"/> the inventor <input checked="" type="checkbox"/> the agent <input type="checkbox"/> the common representative				
Name and Address LEAROYD, Stephanie, A. Glaxo Wellcome plc Glaxo Wellcome House Berkeley Avenue Greenford Middlesex UB6 0NN United Kingdom	State of Nationality		State of Residence	
	Telephone No. 020 8966 8000			
	Facsimile No. 020 8966 8838			
	Teleprinter No.			
2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:				
<input type="checkbox"/> the person <input type="checkbox"/> the name <input checked="" type="checkbox"/> the address <input type="checkbox"/> the nationality <input type="checkbox"/> the residence				
Name and Address LEAROYD, Stephanie, A. GlaxoSmithKline Corporate Intellectual Property Two New Horizons Court Brentford Middlesex TW8 9EP United Kingdom	State of Nationality		State of Residence	
	Telephone No. 020 8966 8412			
	Facsimile No. 020 8966 8838			
	Teleprinter No.			
3. Further observations, if necessary:				
4. A copy of this notification has been sent to:				
<input checked="" type="checkbox"/> the receiving Office <input type="checkbox"/> the International Searching Authority <input type="checkbox"/> the International Preliminary Examining Authority		<input type="checkbox"/> the designated Offices concerned <input checked="" type="checkbox"/> the elected Offices concerned <input type="checkbox"/> other:		

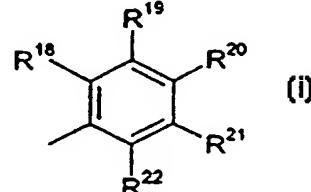
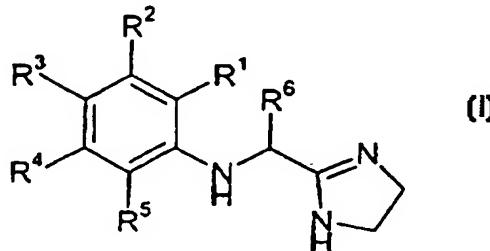
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Beate Giffo-Schmitt Telephone No.: (41-22) 338.83.38
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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : C07D 233/24, A61K 31/417, A61P 43/00, C07D 409/12, 403/12, 401/12, 405/12, 413/12, 417/12		A1	(11) International Publication Number: WO 00/66563 (43) International Publication Date: 9 November 2000 (09.11.00)
(21) International Application Number: PCT/EP00/03848		SPEAKE, Jason, D. [US/US]; Glaxo Wellcome Inc., Five Moore Drive, Research Triangle Park, NC 27709 (US).	
(22) International Filing Date: 28 April 2000 (28.04.00)		(74) Agent: LEAROYD, Stephanie, A.; Glaxo Wellcome plc, Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).	
(30) Priority Data: 9910110.7 30 April 1999 (30.04.99) GB		(81) Designated States: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(71) Applicant (for all designated States except US): GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).		Published With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.	
(72) Inventors; and (75) Inventors/Applicants (for US only): BIGHAM, Eric, Cleveland [US/US]; Glaxo Wellcome Inc., Five Moore Drive, Research Triangle Park, NC 27709 (US). BISHOP, Michael, Joseph [US/US]; Glaxo Wellcome Inc., Five Moore Drive, Research Triangle Park, NC 27709 (US). DREWRY, David, Harold [US/US]; Glaxo Wellcome Inc., Five Moore Drive, Research Triangle Park, NC 27709 (US). GARRISON, Deanna, Trojan [US/US]; Glaxo Wellcome Inc., Five Moore Drive, Research Triangle Park, NC 27709 (US). HODSON, Stephen, Joseph [US/US]; Glaxo Wellcome Inc., Five Moore Drive, Research Triangle Park, NC 27709 (US). NAVAS III, Frank [US/US]; Glaxo Wellcome Inc., Five Moore Drive, Research Triangle Park, NC 27709 (US).			

(54) Title: IMIDAZOLINE DERIVATIVES AS ALPHA-1A ADRENOCEPTOR LIGANDS



(57) Abstract

Compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof are disclosed. Formula (I) wherein R², R³, R⁴ and R⁵ are independently H, halogen, -OH, -C₁₋₃alkyl, -C₁₋₃alkoxy, -SC₁₋₂alkyl, or -CF₃, with the proviso that at least 2 of R², R³, R⁴ and R⁵ are H; R⁶ is H or -CH₃; R¹ is -S(O)_nR⁷ where n is 1 or 2, -S(O)₂NHR⁸, -C(O)R⁹, -NR¹⁴R¹⁵, -C(R¹⁷)=NOR¹⁶, (a) or a 5,6, or 7 membered heteroalkyl or heteroaryl group optionally substituted. Such compounds are useful in the treatment of Alpha-1A mediated diseases or conditions such as urinary incontinence.

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
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BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
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CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
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DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

Int'l Application No
PCT/EP 00/03848

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C07D233/24	A61K31/417	A61P43/00	C07D409/12	C07D403/12
	C07D401/12	C07D405/12	C07D413/12	C07D417/12	

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WALFRED S. SAARI ET AL.: "alpha-Adrenergic activities of some substituted 2-(aminoethyl)imidazolines" JOURNAL OF MEDICINAL CHEMISTRY., vol. 26, no. 12, - 1983 pages 1769-1772, XP002147365 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623 cited in the application * complete document *	1,19,20, 22
A	US 3 754 002 A (RICHARD E. BROWN) 21 August 1973 (1973-08-21) * complete document *	1,19,20, 22
A	US 4 506 074 A (MERCK & CO., INC.) 19 March 1985 (1985-03-19) column 1 -column 3	1,19,20, 22
	-/-	

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

14 September 2000

Date of mailing of the international search report

10/10/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Van Bijlen, H

INTERNATIONAL SEARCH REPORT

Int'l Application No

PCT/EP 00/03848

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0 887 346 A (F. HOFFMANN-LA ROCHE AG) 30 December 1998 (1998-12-30) claims 1,17	1,19,20, 22

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int'l Application No

PCT/EP 00/03848

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
US 3754002	A 21-08-1973	NONE		
US 4506074	A 19-03-1985	ZA 8308259	A	26-06-1985
EP 887346	A 30-12-1998	AU 713068	B	25-11-1999
		AU 7310298	A	24-12-1998
		BR 9802201	A	25-05-1999
		CA 2240136	A	23-12-1998
		CN 1203228	A	30-12-1998
		CZ 9801974	A	13-01-1999
		HR 980353	A	30-04-1999
		HU 9801357	A	28-09-1999
		JP 2977536	B	15-11-1999
		JP 11071353	A	16-03-1999
		NO 982884	A	28-12-1998
		NZ 330506	A	28-10-1999
		PL 326959	A	04-01-1999
		US 5952362	A	14-09-1999
		ZA 9805266	A	06-01-1999

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

14

Applicant's or agent's file reference PU3650/WO	FOR FURTHER ACTION		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP00/03848	International filing date (day/month/year) 28/04/2000	Priority date (day/month/year) 30/04/1999	
International Patent Classification (IPC) or national classification and IPC C07D233/24			
<p>Applicant GLAXO GROUP LIMITED et al.</p> <p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p> <p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input type="checkbox"/> Certain documents cited VII <input checked="" type="checkbox"/> Certain defects in the international application VIII <input type="checkbox"/> Certain observations on the international application 			

Date of submission of the demand 21/11/2000	Date of completion of this report 26.02.2001
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer vanVoorsttotVoorst,M Telephone No. +49 89 2399 8280



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/03848

I. Basis of the report

1. This report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):

Description, pages:

1-63 as originally filed

Claims, No.:

1-29 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- the language of publication of the international application (under Rule 48.3(b)).
- the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- contained in the international application in written form.
- filed together with the international application in computer readable form.
- furnished subsequently to this Authority in written form.
- furnished subsequently to this Authority in computer readable form.
- The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- the description, pages:
- the claims, Nos.:
- the drawings, sheets:

5. This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/03848

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
 - the entire international application.
 - claims Nos. 15-17.

because:

- the said international application, or the said claims Nos. 15-17 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
 - the written form has not been furnished or does not comply with the standard.
 - the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 1-29
	No:	Claims
Inventive step (IS)	Yes:	Claims 1-29
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 1-14,18-29

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP00/03848

No: Claims

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

AD SECTION III:

1. For the assessment of the present claims 15-17 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment. Claims 15-17 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

AD SECTION V:

1. The following documents cited in the International Search Report were considered;
D1: WALTER S. SAARI ET AL.: 'alpha-Adrenergic activities of some substituted 2-(aminoethyl)imidazolines' JOURNAL OF MEDICINAL CHEMISTRY., vol. 26, no. 12, - 1983 pages 1769-1772, cited in the application
D2: US 3 754 002 A (RICHARD E. BROWN), cited in the application
D3: US 4 506 074 A (MERCK & CO., INC.)
D4: EP 0 887 346 A (F. HOFFMANN-LA ROCHE AG), cited in the application.
2. Having regard to this prior art the subject-matter claimed appears to be novel, the compounds disclosed in D1 differ from the present compounds on account of the meaning for X, the compounds disclosed in D2 differ on account of the COOR-group, the compounds of D3 are pyridyl derivatives and the compounds disclosed in D4 differ in the meanings for A and Y.
Thus the subject-matter according to claims 1-29 appears to meet the requirements of Article 33(2) PCT.
3. Closest prior art comprises the compounds disclosed in D1 to D4. D1 describes the profiles of monoaryl derivatives, these being either alpha-1/alpha-2-agonists

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/EP00/03848

or mixed alpha-1-agonists/alpha-2-antagonists, D2 discloses compounds which stimulate the alpha-adrenergic nervous system of mammals and can therefore be used to increase blood pressure, the compounds of D3 possess alpha-2-antagonistic/alpha-1-agonistic properties being useful as antidepressants and nasal decongestants and D4 discloses compound having alpha-1A-agonistic activities, which possess similar activities as the present compounds.

The problem to be solved was to provide certain compounds which are alpha-1A agonists, which can be used in the treatment of urinary incontinence, nasal congestion, priapism, depression, anxiety, dementia, senility, Alzheimer's, deficiencies in attentiveness and cognition and eating disorders.

Having regard to the prior art mentioned above it is considered that this problem has been solved by the compounds of the present application in an inventive manner, since the skilled person could not have expected that the present phenyl-aminoalkyl-2-imidazoline derivatives would show this activity as demonstrated by the Applicant on pages 62/63 of the description.

Thus the subject-matter according to claims 1-29 appears to meet the requirements of Article 33(3) PCT.

4. No objections with regard to Article 33(4) PCT arise for claims 1-14 and 18-29, however see Section III above.

AD SECTION VII:

1. The units "psi" employed on page 10, 17, 18 and 38 are not additionally expressed in terms of the units stipulated by Rule 10.1(a) PCT.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PU3650/WO	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 00/ 03848	International filing date (day/month/year) 28/04/2000	(Earliest) Priority Date (day/month/year) 30/04/1999
Applicant GLAXO GROUP LIMITED et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

contained in the international application in written form.

filed together with the international application in computer readable form.

furnished subsequently to this Authority in written form.

furnished subsequently to this Authority in computer readable form.

the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. Certain claims were found unsearchable (See Box I).

3. Unity of Invention is lacking (see Box II).

4. With regard to the title,

the text is approved as submitted by the applicant.

the text has been established by this Authority to read as follows:

IMIDAZOLINE DERIVATIVES AS ALPHA-1A ADRENOCEPTOR LIGANDS

5. With regard to the abstract,

the text is approved as submitted by the applicant.

the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

as suggested by the applicant.

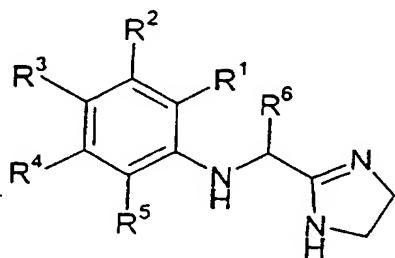
because the applicant failed to suggest a figure.

because this figure better characterizes the invention.

None of the figures.

Box III TEXT OF THE ABSTRACT (Continuation of item 5 of the first sheet)

Compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof are disclosed.

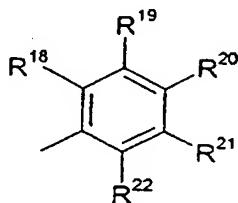


(I)

wherein R², R³, R⁴, and R⁵ are independently H, halogen, -OH, -C₁₋₃alkyl, -C₁₋₃alkoxy, -SC₁₋₂alkyl, or -CF₃, with the proviso that at least 2 of R², R³, R⁴, and R⁵ are H;

R⁶ is H or -CH₃;

R¹ is -S(O)_nR⁷ where n is 1 or 2, -S(O)₂NHR⁸, -C(O)R⁹, -NR¹⁴R¹⁵, -C(R¹⁷)=NOR¹⁶,



or a 5, 6, or 7 membered heteroalkyl or heteroaryl group optionally substituted

Such compounds are useful in the treatment of Alpha-1A mediated diseases or conditions such as urinary incontinence.

INTERNATIONAL SEARCH REPORT

International Application No

EP 00/03848

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7	C07D233/24	A61K31/417	A61P43/00	C07D409/12	C07D403/12
	C07D401/12	C07D405/12	C07D413/12	C07D417/12	

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>WALFRED S. SAARI ET AL.: "alpha-Adrenergic activities of some substituted 2-(aminoethyl)imidazolines" JOURNAL OF MEDICINAL CHEMISTRY., vol. 26, no. 12, - 1983 pages 1769-1772, XP002147365 AMERICAN CHEMICAL SOCIETY. WASHINGTON., US ISSN: 0022-2623 cited in the application * complete document *</p> <p>---</p>	1, 19, 20, 22
A	<p>US 3 754 002 A (RICHARD E. BROWN) 21 August 1973 (1973-08-21) * complete document *</p> <p>---</p>	1, 19, 20, 22
A	<p>US 4 506 074 A (MERCK & CO., INC.) 19 March 1985 (1985-03-19) column 1 -column 3</p> <p>---</p>	1, 19, 20, 22
		-/-

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
 "E" earlier document but published on or after the international filing date
 "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
 "O" document referring to an oral disclosure, use, exhibition or other means
 "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No

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